UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION

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Subject: **Metaflumizone:** Revised Occupational and Residential Exposure/Risk Assessment for Proposed Use as a Granular Fire Ant Bait

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Note: This document supersedes D367561 (M. Dow, 07-Dec-09). An immunotoxicity study has been received and reviewed by the Agency and updates have been made to the Food Quality Protection Act (FQPA) Safety Factor (SF).

BASF Corporation has proposed a Section 3 Registration for application of metaflumizone as a granular fire ant bait in citrus orchards, tree nut orchards, grape vineyards, nonbearing stone and pome fruit orchards and in nurseries containing nonbearing container- or field-grown stone and pome fruit tree stock. The end-use product is Altrevin Fire Ant Bait Insecticide (EPA Reg #7969-xxx), containing 0.063% metaflumizone. No residential uses are being requested at this time.

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1.0 Executive Summary

The Health Effects Division (HED) has conducted an occupational exposure assessment for the proposed use of the insecticide active ingredient (a.i.) metaflumizone as a granular fire ant bait in citrus orchards, tree nut orchards, grape vineyards, nonbearing stone and pome fruit orchards and in nurseries containing nonbearing container- or field-grown stone and pome fruit tree stock. The end-use product is Altrevin Fire Ant Bait Insecticide (EPA Reg #7969-xxx), containing 0.063% metaflumizone. The label specifies that the product is to be applied as a soil treatment. The maximum application rate proposed for broadcast applications is 0.001 lb ai/A, and for individual mound treatments is 0.000078 lb ai/mound.

The short-(1-30 days), and intermediate-(1-6 months) term dermal toxicological point of departure is a no-observed-adverse-effect-level (NOAEL) of 100 mg/kg/day identified from a 90-day dermal study in the rat. The short- and intermediate-term inhalation toxicological point of departure is a lowest-observed-adverse-effect-level (LOAEL) of 0.03 mg/L (8 mg/kg/day) identified from a 28-day inhalation study in the rat. The Food Quality Protection Act Safety Factor (FQPA SF) is being retained as an uncertainty factor for the use of a LOAEL in the absence of a NOAEL for *inhalation exposure scenarios*. The total uncertainty factor that has been applied to occupational and residential risk assessments is 100 for short- and intermediate-term dermal exposures and 1000 for short- and intermediate-term inhalation exposures.

The current proposed use is not expected to result in residential exposure; however, metaflumizone is currently registered as a fire ant bait for use on residential and golf course turf and as a pet spot-on product. An assessment was previously conducted to assess residential handler and post-application exposure/risk from the fire ant bait use and the pet care use. No risks of concern were identified (i.e., Margins of Exposure (MOEs) > 100). In addition, a concurrent action was submitted for use of metaflumizone as a granular fly bait. The proposed product could be used in areas where children could be present; therefore, a residential assessment was performed. None of the post-application scenarios assessed resulted in risks of concerns (i.e., MOEs > 100).

The occupational handler assessment for the proposed uses was completed assuming the maximum label application rate. Broadcast applications were assumed to be made by tractor-drawn spreaders, belly grinders, and/or push-type spreaders. Individual mound applications were assumed to be made by a cup/spoon or by hand. Based on the activity use pattern, the duration of exposure is expected to be short-term and intermediate-term for occupational scenarios; long-term exposures (greater than 6 months) are not anticipated based on the proposed use pattern. The same endpoints are used for short- and intermediate-term exposures; therefore, risks are the same for all durations of exposure. The proposed label requires long-sleeved shirt and long pants and chemical-resistant gloves as dermal PPE for all applicators and other handlers.

Occupational handler dermal and inhalation risk estimates were calculated. The dermal and inhalation exposure risks for mixer/loaders, applicators, and mixer/loader/applicators are not of

concern (i.e., MOEs >100 for dermal and >1000 for inhalation) at baseline and with the addition of gloves as recommended by the label. Occupational dermal postapplication exposure was not assessed as it is not anticipated that workers will be exposed after application of the fire ant bait. Applications are to be soil-directed and post-application exposure is believed to be negligible since there will be limited dermal contact with treated surfaces. In addition, workers are not expected to frequent areas infested with active fire ants.

Review of Human Research

This risk assessment relies in part on data from studies in which adult human subjects were intentionally exposed to a pesticide to determine their dermal and inhalation exposure. Many such studies, involving exposure to many different pesticides, comprise generic pesticide exposure databases such as the Pesticide Handlers Exposure Database (PHED), the Agricultural Handlers Exposure Task Force (AHETF) and the Agricultural Reentry Task Force (ARTF) Database. EPA has reviewed all the studies in these multi-pesticide generic exposure databases, and on the basis of available evidence has found them to have been neither fundamentally unethical nor significantly deficient relative to standards of ethical research conduct prevailing when they were conducted. There is no regulatory barrier to continued reliance on these studies, and all applicable requirements of EPA's Rule for the Protection of Human Subjects of Research (40 CFR Part 26) have been satisfied.

2.0 Hazard Profile

Metaflumizone demonstrated low acute toxicity (Category IV) via the oral, dermal, and inhalation routes. It is neither a dermal irritant (Category IV), eye irritant (Category IV), nor a dermal sensitizer. Table 2.0.1 presents a summary of the acute toxicity information for metaflumizone.

Table 2.0.1. Acute Toxicity Profile - Metaflumizone Technical (96% ai).

Guideline No./Study Type	MRID No.	Results	Toxicity Category
Metaflumizone Technical (96% ai)			
870.1100/Acute oral toxicity rat	46264232	LD_{50} => 5,000 mg/kg (males, females combined)	IV
870.1100/Acute oral toxicity mouse	46264234	LD_{50} => 5,000 mg/kg (males, females combined)	IV
870.1200/Acute dermal toxicity rat	46264235	LD_{50} > 5,000 mg/kg (males, females combined)	IV
870.1300/Acute inhalation toxicity rat	46264236	LC_{50} > 5.2 mg/L (males, females combined)	IV
870.2400/Primary eye irritation rabbit	46264238	Conjunctivitis in 2/3, 1/3, 0/3 at 1, 24, and 48 hours, resp.; no positive effects	IV
870.2500/Primary dermal irritation rabbit	46264237	non-irritant PII = 0	IV
870.2600/Dermal sensitization guinea pig	46264239	is not a sensitizer	N/A

The short- and intermediate-term incidental oral toxicological point of departure was identified from a 2-generation reproduction study in the rat; where the maternal LOAEL was 50 mg/kg/day based on poor health state and decreased bodyweight. The NOAEL was 20 mg/kg/day.

The short- and intermediate-term dermal toxicological point of departure was identified from a 90-day dermal study in the rat, where the LOAEL was 300 mg/kg/day based on decreased body-

weight gain and food consumption in males and females; anogenital smearing, decreased body weight, increased macrophages in the thymus, lymphocyte necrosis in the mesenteric lymph nodes, diffuse atrophy of the mandibular lymph node, and increased hemosiderin in the liver of females. The NOAEL was 100 mg/kg/day.

The short- and intermediate-term inhalation toxicological point of departure was identified from a 28-day inhalation study in the rat, where the LOAEL was 0.03 mg/L (8 mg/kg/day)[1] based on lymphocyte necrosis in the mesenteric lymph node in females.

Metaflumizone was classified as a "not likely" human carcinogen.

A summary of the toxicological endpoints and points of departure chosen for the relevant exposure scenarios for human risk assessment are found in Table 2.0.2.

Table 2.0.2. Summary of Toxicological Doses and Endpoints for Metaflumizone Used in Occupational Exposure Assessment.[1]

Exposure Scenario	Dose Used in Risk Assessment, UF	FQPA SF or LOC for Risk Assessment	Study and Toxicological Effects
Acute Dietary- general population, including infants and children	N/A	N/A	An endpoint of concern (effect) attributable to a single dose was not identified in the database. Quantification of acute risk to general population including infants and children is not required.
Short- (1-30 days) and Intermediate- (1-6 months) Term Incidental Oral	NOAEL = 20 mg/kg/day	LOC (residential) = MOE < 300	2-generation reproduction (rat); Maternal LOAEL = 50 mg/kg/day based on poor health state and decreased bodyweight.
Short- (1-30 days) and Intermediate-(1-6 months) Term Dermal	NOAEL = 100 mg/kg/day	LOC (residential) = MOE < 100 LOC (occupational) = MOE < 100	90-day dermal (rat); LOAEL = 300 mg/kg/day based on decreased BW gain and food consumption (M&F); anogenital smearing, decreased BW, increased macrophages in the thymus, lymphocyte necrosis in the mesenteric lymph nodes, diffuse atrophy of the mandibular lymph node, and increased hemosiderin in the liver (F).
Short- (1-30 days) and Intermediate- (1-6 months) Term Inhalation	LOAEL = 0.03 mg/L[2] NOAEL not observed	LOC (residential) = MOE < 1000 (includes 10x FQPA SF in form of UF_L) LOC (occupational) = MOE < 1000 (includes 10x UF_L)	28-day inhalation (rat); LOAEL = 0.03 mg/L* based on lymphocyte necrosis in the mesenteric lymph node (F).
Cancer (oral, dermal, inhalation)	**Classification:** Not likely to be carcinogenic to humans.		

[1] UF = uncertainty factor, FQPA SF = FQPA Safety Factor, NOAEL = no-observed adverse-effect level, LOAEL = lowest-observed adverse-effect level, MOE = margin of exposure, LOC = level of concern, UF_{DB} = database uncertainty factor, UF_L = uncertainty factor for lack of a NOAEL

[2] 0.03 mg/L x 100% absorption x 45.2 L/hr/kg (conversion factor) x 6 hrs/day (exposure duration) x 1 (activity factor) = 8 mg/kg bw/day

[1] 0.03 mg/L × 100% absorption × 45.2 L/hr/kg (conversion factor) × 6 hrs/day (exposure duration) × 1 (activity factor) = 8 mg/kg/day

The Agency's level of concern for risks (i.e., target level for MOE) is defined by the uncertainty factors that are applied to the assessment. The Agency typically applies a factor of 10x to account for interspecies extrapolation to humans from the animal test species and another factor of 10x to account for intra-species sensitivity. For the dermal exposure scenarios, the level of concern (LOC) is 100 based on a combined uncertainty factor (UF) of 100 for interspecies (10x) and intraspecies (10x) extrapolation. For the inhalation exposure scenarios, since a NOAEL was not achieved in the 28-day inhalation toxicity study in rats, and this study was the most relevant for inhalation exposure scenarios, the FQPA SF is being retained as an uncertainty factor for the use of a LOAEL in the absence of a NOAEL (UF_L), resulting in a combined uncertainty factor of 1000. For the incidental oral scenarios, a combined uncertainty factor (UF) of 300 was applied to account for interspecies (10x) and intraspecies (10x) extrapolation and an FQPA SF of 3x to account for the 2-fold greater absorption observed in dietary exposures (see detailed explanation in Memo, K. Lowe *et. al*, D393447).

3.0 Use Profile

The proposed product, Altrevin Fire Ant Bait Insecticide, is a 0.063% active ingredient solid bait formulation proposed as a soil treatment for fire ants in citrus orchards, tree nut orchards, grape vineyards, nonbearing stone and pome fruit orchards and in nurseries containing nonbearing container- or field-grown stone and pome fruit tree stock. The label allows for broadcast and individual mound applications. The restricted entry interval (REI) specified on the label is 12 hours. The use profile proposed for this Section 3 registration is summarized in Table 3.0.

Table 3.0. Summary of Directions for Use of Metaflumizone.

Application Timing	Apply as curative treatment at first sign of fire ant activity
Type	Broadcast or individual mound treatment
Application Method	Tractor-drawn spreader, push-type spreader, belly grinder, cup/spoon, by hand
Formulation [EPA Reg. No.]	Solid ant bait [7969-xxx]
Maximum Application Rate	Broadcast: 0.001 lb ai/A Mound: 0.000078 lb ai/mound
Maximum Number of Applications per Season	4
Maximum Seasonal Application Rate (lb ai/A)	0.004
PHI (days)	5 days for citrus trees, nut trees and grapes 1 year for soil around non-bearing stone and pome fruit trees
Use Directions and Limitations	Retreat after 4-8 weeks Distribute bait uniformly around perimeter of mound; DO NOT disturb mound DO NOT water-in granules after application

4.0 Residential (Non-Occupational) Exposure/Risk Characterization

The proposed use is as a fire ant bait product in agricultural settings and, therefore, will not result in residential exposure; however, there are already registered fire ant bait uses and pet uses that would result in residential exposure that have been previously assessed (D345154, T. Bloem *et al.*, 26-Jan-2010; D315785, M. Dow, 19-Jan-2006). The fire ant bait product is registered for use on residential and golf course turf. The pet use is a spot-on pet product to control fleas and ticks. It should be noted that the pet use currently registered for metaflumizone is in the process of being cancelled; however, the use has been included in this risk assessment. Existing stock of the registered product will continue to be sold, but registration will not be maintained beyond 2012. In addition, a concurrent action was submitted for use of metaflumizone as a granular fly bait (D393548, K. Lowe, 20-Sep-2011). That proposed product can be used in areas where children could be present (e.g., campgrounds, picnic grounds) and, therefore, a residential assessment was performed.

4.1 Residential Handler Exposure

Fire Ant Bait (registered on lawns, landscapes, golf courses, and other non-cropland): Residential handler exposure was expected for homeowners who apply the fire ant bait products to home lawns. Since the residential and commercial fire ant products have identical application rates, HED used the commercial loader/applicator dermal (no gloves) and inhalation exposure assumptions to calculate exposure and risk estimates for the homeowner loader/applicator scenario (commercial push-type drop spreader; 5 acres/day; only short-term exposures anticipated). Risks were not a concern for residential handlers (i.e., MOEs > the LOC of 100 for dermal exposures and 1000 for inhalation exposures; see Table 4.4).

Pet Care (registered spot-on product): Exposure/risk from metaflumizone application to domestic pets was not assessed because handler contact is expected to be negligible. The spot-on product is designed to be self-contained as it is applied directly from the tube to the pet with the tip of the applicator used to part the pet's hair.

Fly Bait (proposed): The proposed product is not intended for homeowner use as it is proposed for commercial/recreational areas such as campgrounds and picnic grounds. It is expected that commercial handlers would apply this product to areas such as these. Therefore, a residential handler assessment has not been performed for the proposed fly bait product.

4.2 Residential Post-application Exposure

Fire Ant Bait (registered on lawns, landscapes, golf courses, and other non-cropland): Use of the fire ant products may result in short-term post-application exposure to children (3 to <6 year olds; dermal and incidental oral), adults (dermal), and adolescents (dermal). Ingestion of metaflumizone granules found in treated lawns or gardens is also a potential source of exposure for children. This scenario is considered an episodic event by HED and, therefore, is assessed as

an acute exposure (i.e., acute dietary endpoints are used). Since there is no acute dietary endpoint applicable to children, no quantitative assessment was needed. The resulting dermal and incidental oral MOEs were greater than the LOCs of 100 and 300, respectively, and, therefore, were not of concern (see Table 4.4).

Pet Care (registered spot-on product): The pet care products may also result in post-application dermal (all populations) and incidental oral [children (3 to<6 year olds)] exposures. The resulting MOEs are >100 and >300 for dermal and incidental oral exposures, respectively, therefore, exceed HED's LOC (see Table 4.4). HED notes that pet care product exposure calculations can be considered refined in that they are based on the assumptions that 0.78% of the application rate is available as dislogeable residue rather than the default 20%; for further information see D315785 (M. Dow, 19-Jan-2006).

Fly Bait (proposed): Use of the proposed fly bait product may result in short-term post-application exposure to children (3 to <6 year olds; dermal and incidental oral) and adults (dermal). Ingestion of metaflumizone granules found in treated lawns or gardens is also a potential source of exposure for children. This scenario is considered an episodic event by HED and, therefore, is assessed as an acute exposure (i.e., acute dietary endpoints are used). Since there is no acute dietary endpoint applicable to children, no quantitative assessment was needed. The resulting dermal and incidental oral MOEs were greater than the LOC of 100 and 300, respectively, and, therefore, were not of concern (see Table 4.4).

4.4 Combined Residential Exposure

For residential handlers, dermal and inhalation exposures are combined since the endpoints are similar for these routes. For children (3 to <6 year olds), post-application hand-to-mouth and dermal exposures are combined. Dermal exposure could be combined with all the incidental oral exposure scenarios (e.g., hand-to-mouth, object-to-mouth, soil ingestion) since it is assumed that these exposures do not occur as single, isolated events, but rather as a series of concurrent events that may overlap. However, combining all of the incidental oral exposures with dermal exposure would be overly conservative because each of these scenarios, independently, incorporates high-end, health protective inputs or assumptions. Combining post-application dermal exposure with only hand-to-mouth exposure is considered a protective estimate of children's exposure to pesticides used in residential settings.

Since the LOCs for the dermal, inhalation and incidental oral routes are not the same (dermal LOC = 100, inhalation LOC = 1000, and incidental oral LOC = 300), these routes were combined using the aggregate risk index (ARI) approach.

Table 4.4. Summary of Short-term Residential Handler and Post-application Exposures and Risks.

Population	Route of Exposure	Dose (mg/kg/day)	MOE[1]
Fire Ant Bait (registered on lawns, landscapes, golf courses, and other non-cropland; D345154/D315785)			
Adult -- Residential Handler	Dermal	0.00021	480,000

Table 4.4. Summary of Short-term Residential Handler and Post-application Exposures and Risks.			
Population	Route of Exposure	Dose (mg/kg/day)	MOE[1]
	Inhalation	0.00000045	18,000,000
	Combined dermal and inhalation	--	ARI[2] = 3,800
Adult – Residential Post-application	Dermal	0.000232	430,000
Adult – Golfer Post-application	Dermal	0.000016	6,200,000
Adolescent – Golfer Post-application	Dermal	0.0000272	3,700,000
Children (3 to <6 year olds) – Post-application	Incidental oral hand-to-mouth	0.000015	1,300,000
	Incidental oral object-to-mouth	0.00000093	22,000,000
	Dermal	0.00039	260,000
	Combined incidental oral hand-to-mouth and dermal	--	ARI[3] = 1,600
Pet Care (registered spot-on; D345154/D315785)			
Adults – Post-application	Dermal	0.29	340
Children (3 to <6 year olds) – Post-application	Incidental oral hand-to-mouth	0.035	570
	Dermal	0.16	620
	Combined incidental oral hand-to-mouth and dermal	--	ARI[3] = 1.5
Fly Bait (proposed; D393548)			
Adult –Post-application	Dermal	0.0033	31,000
Children (3 to <6 year olds) – Post-application	Incidental oral hand-to-mouth	0.00021	96,000
	Incidental oral object-to-mouth	0.000052	380,000
	Incidental soil ingestion	0.0000007	29,000,000
	Dermal	0.0054	18,000
	Combined incidental oral hand-to-mouth and dermal	--	ARI[3] = 120

1. MOE = NOAEL (mg/kg/day) ÷ Dose (mg/kg/day).
2. ARI = Aggregate Risk Index = $1 \div ((1 \div (MOE_{inhalation} \div LOC_{inhalation})) + (1 \div (MOE_{dermal} \div LOC_{dermal})))$; ARI > 1 indicates an acceptable exposure.
3. ARI = Aggregate Risk Index = $1 \div ((1 \div (MOE_{incidental\ oral\ hand\text{-}to\text{-}mouth} \div LOC_{incidental\ oral\ hand\text{-}to\text{-}mouth})) + (1 \div (MOE_{dermal} \div LOC_{dermal})))$; ARI > 1 indicates an acceptable exposure.

5.0 Occupational Exposure/Risk Characterization

5.1 Short- and Intermediate-Term Handler Risk

Based on the anticipated use patterns and current labeling, types of equipment and techniques that can potentially be used, occupational handler exposure is expected from the proposed uses. The quantitative exposure/risk assessment developed for occupational handlers is based on the following scenarios:

Mixer/Loader:
(1) loading granules for tractor-drawn spreader applications,

Applicator:
(2) applying granules via tractor-drawn spreader,
(3) applying granules by hand,

Mixer/Loader/Applicator:
(4) loading/applying granules via "push type" rotary spreader,
(5) applying ready-to-use granules by spoon (Proprietary study), and
(6) loading/applying granules via belly grinder.

For pesticide handlers, HED presents estimates of dermal exposure for "baseline" (i.e., workers wearing a single layer of work clothing consisting of a long sleeved shirt, long pants, shoes plus socks and no protective gloves), as well as for "baseline" and the use of protective gloves or other personal protective equipment (PPE), as might be necessary. The metaflumizone product labels direct mixers, loaders, applicators and other handlers to wear long-sleeved shirt and long pants, chemical-resistant gloves, and shoes plus socks.

No chemical-specific handler exposure data were submitted in support of this Section 3 registration. One proprietary study was available to use as surrogate data for the spoon/cup scenario. The study used for the spoon scenario is described below.

For the other scenarios assessed, HED has relied on the most scientifically-reliable surrogate data currently available from various sources such as the Pesticide Handler Exposure Database (PHED), the Agricultural Handler Exposure Task Force (AHETF), and the Outdoor Residential Exposure Task Force (ORETF). Some of this data, such as the industry task force data, is compensatory, subject to the data protection provisions of FIFRA. HED policy on use of surrogate data is described in more detail on the Agency's website (http://www.epa.gov/pesticides/science/handler-exposure-data.html). Scenario-specific surrogate exposure data, including their sources, are presented in the "Occupational Pesticide Handler Unit Exposure Surrogate Reference Table" (http://www.epa.gov/pesticides/science/handler-exposure-table.pdf).

Proprietary study

Worker Exposure Study During Application of Regent 20GR In Banana Plantation, EPA MRID 452507-02 (Fipronil Study): Exposure during the application of a granular formulation of the insecticide, fipronil (i.e., Regent 20GR), was monitored during spoon applications to bananas for control of insects, mites, and nematodes. A total of 10 mixer/loader/applicator events spoon application to bananas were monitored during applications on two different days in June, 1994, on the same banana plantation in Cameroon. The replicates were as follows: 6 spoon/hand applications on day 1; and 4 spoon/hand applications on day 2. Weather was typical of the application season in that it was hot and humid.

Monitoring was completed using whole body dosimeters, cotton gloves, cotton caps, and personal sampling pumps equipped with filters. Regent 20GR was supplied in 22 pound boxes, which were loaded directly into buckets for the spoon applicators. The application rate for fipronil used in this study is 7.5 grams of Regent 20GR (i.e., 0.15 grams ai/plant), which is equivalent to about 0.26 lb ai/acre (0.00033 lb ai/plant) at approximately 800 plants per acre. The numbers of acres treated ranged from approximately 0.75 to 1 acre. The pounds of active ingredient handled ranged from about a quarter to half a pound per replicate.

Each applicator wore whole body dosimeters that also served as the normal work clothing. PVC gloves were also worn over cotton gloves which served as the dosimeters. A protection factor of 50 percent was used by the Agency

to calculate exposure levels under a layer of normal work clothing. Dosimeter samples were segmented into arms, legs, and torso for analysis.

Unit Exposure Values Obtained From MRID 452507-02		
Scenario Monitored	Dermal (mg exp./lb ai handled) Single Layer Clothing (short sleeves and shorts)	Inhalation (µg exp./lb ai handled)
Applications with a Spoon	3.5	45

This fipronil study is considered to be an appropriate source of surrogate handler exposure data because formulation types are similar (granular) and application methods are similar (applying granulars with a spoon) to the proposed use. The study is considered to be of sufficient quality for use in risk assessment. Data compensation for these data should be determined.

Typically, HED completes short- and intermediate-term assessments for occupational scenarios in all cases because these kinds of exposures are likely and acceptable use/usage data are not available to justify deleting intermediate-term scenarios. Based on use data and label instructions, HED believes that occupational exposures may occur over a single day or up to weeks at a time for many use-patterns and that intermittent exposure over several weeks may also occur. Some applicators may apply these products over a period of weeks, because they are commercial applicators who are completing multiple applications for multiple clients. Long-term exposures are not expected, therefore, a long-term assessment was not conducted.

The daily areas treated were defined for each handler scenario (in appropriate units) by determining the amount that can be reasonably treated in a single day. When possible, the assumptions for daily areas treated are taken from the HED's ExpoSAC Policy #9: "Standard Values for Daily Acres Treated in Agriculture", which was revised on July 5, 2000. Values used for area treated in each scenario include: 40 acres for applications with tractor drawn spreader, 5 acres for "push-type" spreader applications, 1 acre for belly grinder applications, and 5 mounds for fire ant spot treatments.

A dermal-absorption factor was not needed since the dermal point of departure is based on a dermal study. An inhalation absorption factor of 100% for extrapolation from an oral exposure to an inhalation exposure was assumed. A body weight of 70 kg was used since the endpoints were not related to developmental effects. Daily dermal or inhalation handler exposures are estimated for each applicable handler task with the application rate, the area treated in a day, and the applicable dermal or inhalation unit exposure using the following formula:

Daily Exposure = Unit Exposure x Application Rate x Daily Area Treated

Where:

Daily Exposure	=	Amount (mg/day) deposited on the surface of the skin that is available for dermal absorption or amount inhaled that is available for inhalation absorption;
Unit Exposure	=	Unit exposure value (mg/lb ai) derived from August 1998 PHED data;
Application Rate	=	Normalized application rate based on a logical unit treatment, such as acres (A); and
Daily Area Treated	=	Normalized application area based on a logical unit treatment such as acres

(A/day).

The daily dermal or inhalation dose is calculated by normalizing the daily exposure by body weight and adjusting, if necessary, with an appropriate dermal or inhalation absorption factor using the following formula:

Average Daily Dose = Daily Exposure x Absorption Factor / Body Weight

Where:

Average Daily Dose	=	Absorbed dose received from exposure to a pesticide in a given scenario (mg/kg/day);
Daily Exposure	=	Amount (mg/day) deposited on the surface of the skin that is available for dermal absorption or amount inhaled that is available for inhalation absorption;
Absorption Factor	=	A measure of the amount of chemical that crosses a biological boundary such as the skin or lungs (% of the total available absorbed); and
Body Weight	=	Body weight determined to represent the population of interest in a risk assessment (kg).

Dermal and inhalation risks were combined in this assessment, since the toxicological effects for these exposure routes were similar. A total aggregated risk index (ARI) was used since the target MOE values for dermal exposure (100) and incidental oral exposure (1000) are different. The target ARI is 1; therefore, ARIs of less than 1 are risks of concern. The aggregate risk index (ARI) was calculated as follows.

$$\textit{Aggregate Risk Index (ARI)} = 1 \div (1 \div RI_{dermal}) + (1 \div RI_{inhalation})$$

Where:

Risk Index (RI) = MOE ÷ Uncertainty Factor

Table 5.1.1 presents the exposure/risks for short and intermediate-term dermal and inhalation exposures at baseline and with the addition of gloves as personal protective equipment as recommended on the label. The dermal and inhalation exposure risks for mixer/loaders, applicators and mixer/loader/applicators are not of concern (i.e., MOEs >100 for dermal exposures and 1000 for inhalation exposures) at baseline and with the addition of gloves.

Table 5.1.1. Short-/Intermediate-Term Occupational Exposure and Risk Estimates for Metaflumizone.

Exposure Scenario	Mitigation[1]	Dermal Unit Exposure (ug/lb ai)[2]	Inhalation Unit Exposure (ug/lb ai)[2]	Application Rate[3]	Amount Treated Daily[4]	Dermal		Inhalation		ARI[9]
						Dose (mg/kg/day)[5]	MOE[6]	Dose (mg/kg/day)[7]	MOE[8]	
MIXER/LOADER										
Mixing / Loading Granules for Tractor Drawn Spreader Applications	Baseline	8.4	1.7	0.001 lb ai/acre	40 acres	0.0000048	21,000,000	9.70E-07	8,200,000	7,900
	PPE-G	6.9	NA			0.0000039	25,000,000	NA	NA	35,000
APPLICATOR										
Applying Granules via Tractor Drawn Spreader	Baseline	9.9	1.2	0.001 lb ai/acre	40 acres	0.0000057	18,000,000	6.90E-07	12,000,000	11,000
	PPE-G	7.2	NA			0.0000041	24,000,000	NA	NA	47,000
Applying Granules by Hand	Baseline	104000	470	0.000078 lb ai/mound	5 mounds	0.00058	170,000	2.60E-06	3,100,000	1,100
	PPE-G	71000	NA			0.0004	250,000	NA	NA	2,100
MIXER/LOADER/APPLICATOR										
Mixing / Loading/Applying Granulars via "Push Type" Rotary Spreader	Baseline	440	10	0.001 lb ai/acre	5 acres	0.000031	3,200,000	7.10E-07	11,000,000	8,200
	PPE-G	240	NA			0.000017	5,800,000	NA	NA	28,000
Applying Ready to Use Granular by Spoon (MRID 452507-01)	Baseline	No Data	45	0.000078 lb ai/mound	5 mounds	No Data	No Data	2.50E-07	32,000,000	No Data
	PPE-G	2000	NA			0.000011	9,000,000	NA	NA	58,000
Mixing / Loading/Applying Granulars via Belly Grinder	Baseline	10000	62	0.001 lb ai/acre	1 acre	0.00014	700,000	8.90E-07	9,000,000	3,900
	PPE-G	9300	NA			0.00013	750,000	NA	NA	6,400

[1] Level of mitigation: Baseline and PPE-G (gloves). Gloves are recommended PPE on proposed label.
[2] PHED/ORETF/AHETF or MRID 452507-01
[3] Based on proposed label (Reg. No. #7969-xxx)

[4] Exposure Science Advisory Council Policy #9.1
[5] Dermal Dose = Dermal Unit Exposure (mg/kg) × Application Rate (lb ai/acre or lb ai/mound) × Amount Treated (acres/day or mounds/day) ÷ BW (70 kg)
[6] Dermal MOE = Dermal NOAEL (100 mg/kg/day) ÷ Dermal Dose (mg/kg/day). LOC = 100.
[7] Inhalation Dose = Dermal Unit Exposure (mg/kg) × Application Rate (lb ai/acre) × Amount Treated (acres/day) ÷ BW (70 kg)
[8] Inhalation MOE = Inhalation NOAEL (8 mg/kg/day) ÷ Inhalation Dose (mg/kg/day). LOC = 1000.
[9] ARI (Aggregated Risk Index) = 1 / ((1 ÷ (Dermal MOE ÷ LOC_{dermal})) + (1 ÷ (Inhalation MOE ÷ $LOC_{inhalation}$))). Baseline dermal and PPE-G Dermal combined with Baseline Inhalation.

5.2 Short- and Intermediate-Term Post-Application Risk

HED uses the term post-application to describe exposures that occur when individuals are present in an environment that has been previously treated with a pesticide (also referred to as re-entry exposure). Such exposures may occur when workers enter previously treated areas to perform job functions, including activities related to crop production, such as scouting for pests or harvesting.

5.2.1 Dermal Post-Application Risk

In the case of metaflumizone, post-application dermal exposure is expected to be negligible. Dermal contact with treated surfaces is not expected; all applications are directed towards the soil surface. In addition, workers are not expected to frequent areas infested with active fire ants. For these reasons, a quantitative dermal post-application assessment has not been conducted.

Restricted Entry Interval (REI)
Since a quantitative post-application dermal risk assessment has not been conducted, the default Worker Protection Standard (WPS) REI applies and is based on the acute toxicity category of the technical product for dermal toxicity, skin irritation potential, and eye irritation potential. Metaflumizone has low acute toxicity (Category IV) via the dermal route, and is neither a dermal irritant (Category IV), eye irritant (Category IV), nor a dermal sensitizer. Therefore, the default REI of 12 hours would apply for metaflumizone.

5.2.2 Inhalation Post-Application Risk

Based on the Agency's current practices, a quantitative occupational post-application inhalation exposure assessment was not performed for metaflumizone at this time. However, there are multiple potential sources of post-application inhalation exposure to individuals performing post-application activities in previously treated fields. These potential sources include volatilization of pesticides and resuspension of dusts and/or particulates that contain pesticides. The Agency sought expert advice and input on issues related to volatilization of pesticides from its Federal Insecticide, Fungicide, and Rodenticide Act Scientific Advisory Panel (SAP) in December 2009. The Agency received the SAP's final report on March 2, 2010 (http://www.epa.gov/scipoly/SAP/meetings/2009/120109meeting.html). The Agency is in the process of evaluating the SAP report as well as available post-application inhalation exposure data generated by the Agricultural Reentry Task Force and may, as appropriate, develop policies and procedures, to identify the need for and, subsequently, the way to incorporate occupational

post-application inhalation exposure into the Agency's risk assessments. If new policies or procedures are put into place, the Agency may revisit the need for a quantitative occupational post-application inhalation exposure assessment for metaflumizone.

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